

REMARKS/ARGUMENTS

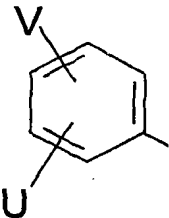
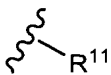
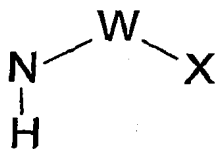
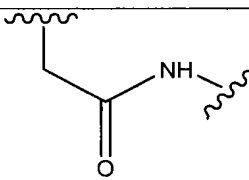
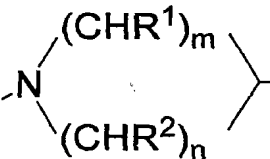
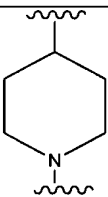
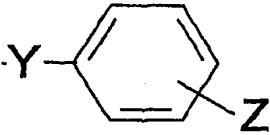
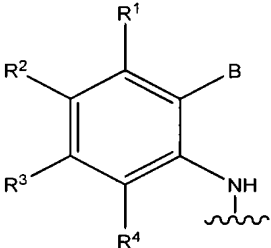
Claims 22-24, 29 and 57-58 are active.

The claims have been amended to remove the term "solvate" thereby rendering the 112, first paragraph rejection inapplicable.

No new matter is added.

The rejection applied under 35 U.S.C. 103 (a) citing the WO 03/010159 description is not sustainable.

Comparing the teachings of WO03/010159 (page 3-4), and the subject-matter of claim 22 makes it clear that there are no overlapping embodiments. To aid the comparison, please see the table below showing structural correspondences of the Markush formulae.

| WO03/0100159 | Claim 22 of the present application |
|---|--|
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|  |  |
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Importantly, there are two provisos in WO03/0100159 on page 4 lines 15-22 to be considered:

acids and bases with the proviso that

when Z means hydrogen atom, Y means -CH₂- group, both of m and n mean 2, both of R¹ and R² mean hydrogen atom, W means -CO- group, X means -CH₂- group and V means hydrogen atom, then the meaning of U is other than a 4-bromo substituent and

when Z means hydrogen atom, Y means -CH₂- group, both of m and n mean 2, both of R¹ and R² mean hydrogen atom, both of W and X mean -CO- group and V means hydrogen atom, then the meaning of U is other than a 4-carboxyl or 4-etoxy carbonyl substituent.

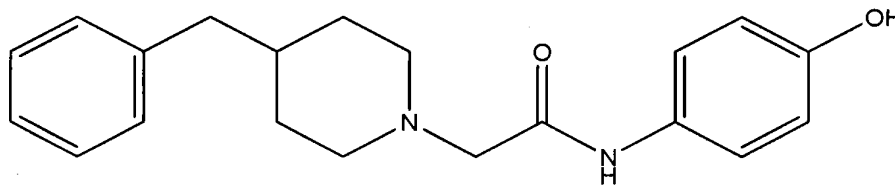
As such, for those compounds of WO03/0100159 where Z is hydrogen –rendering an unsubstituted phenyl– then, Y is necessarily –CH₂–. Such combination or embodiment is not present in claim 22, since an amino group (–NH–) is attached to the phenyl substituted with R¹–R⁴ and B, not the methylene –CH₂– (see last table row above).

Moreover, the counterpart substituents of Z, which are R¹–R⁴–B, will never be all hydrogen, because the definition of B in claim 22 does not include a hydrogen substituent.

In addition, and contrary to what pointed out and underlined in the USPTO Office action, it will be readily noticed that the optionally substituted phenyl claimed under R¹¹ of claim 22 does not include as substituents, any halogen atom, hydroxyl, hydroxymethyl, C₁–C₄alkyl, C₁–C₄alkoxy, nor C₁–C₄alkoxycarbonyl (as provided for V and U in WO03/0100159). Differently, the phenyl substituents of R¹¹, apart from hydrogen, consist of cyclohexyl, phenyl, phenoxy, benzoyl, –C(=O)–C₁₋₂–alkyl, –C(H)(OH)(phenyl) and –C(H)(OH)(CH₃) (hydroxyethyl).

In addition, the apparent closest teaching in WO03/010159 in terms of structural features and for which biological data is provided (see Table 2 row 7 on page 16 of WO03/010159) is the following compound:

2-(4-Benzyl-piperidin-1-yl)-N-(4-hydroxy-phenyl)-acetamide (70002863) of Example 192



This compound differs from the subject-matter of claim 22 still in two structural features:

1. the methylene $\text{-CH}_2\text{-}$ instead of -NH- linking the left phenyl and the following piperidine rings; and
2. the hydroxy substituent of the end phenyl ring, which hydroxy is not encompassed under the phenyl substituents in R^{11} .

Further, the compound (2-(4-Benzyl-piperidin-1-yl)-N-(4-hydroxy-phenyl)-acetamide (70002863)) has the highest ED50 value, which is the least interesting biological activity of those compounds tested in WO03/010159.

As such, there is no hint in WO03/010159 to specifically pick compound 70002863, and modify it structurally in two ways in order to arrive at the subject-matter of claim 22, and expect to obtain valuable compounds in terms of biological activity. (See "Where an invention for which a patent is sought is a compound which is a member of an homologous series and the prior art discloses a *nonadjacent* member of that series, we do not consider the Hass and Henze cases authority for the legal presumption of obviousness of the claimed invention." *In re Elpern*, 326 F.2d. 762, 140 USPQ 224 (CCPA 1964)). In other words, it would not have been obvious to one of ordinary skill in the art at the time of the claimed invention to make these at least two changes in the structure of 70002863 and expect significant biological activities in the nanomolar range.

Withdrawal of the rejection is requested.

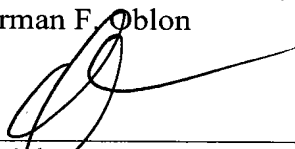
With respect to the provisional rejection citing 10/566,399, in accordance with MPEP § 822.01, If the "provisional" double patenting rejection in the present application is the only

rejection remaining, the examiner should then withdraw that rejection and permit the present application to issue as a patent, thereby converting the "provisional" double patenting rejection in the other application(s) into a double patenting rejection at the time the present application issues as a patent.

It is respectfully submitted that all of the claims are in proper form for allowance. Should any unresolved issues remain, the Examiner is invited to call Applicants' attorney at the telephone number indicated below.

Respectfully Submitted,

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